REMARKS

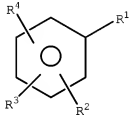
Claim 1 has been amended to require the first active ingredient to be present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate. Support for this amendment may be found, for example, in paragraph [0029] of the published application (U.S. 2004/0266887 A1), as well as in originally filed dependent claim 8. Claims 7 and 8 have now been cancelled. Claims 1-6, 9, 10, 12, 13, and 15-60 will be pending upon entry of this Amendment C and Response after RCE. Applicants respectfully request reconsideration and allowance of all pending claims.

1. Rejection of Claims 1-4,6,9,10 and 15-25 Under 35 U.S.C. §103(a)

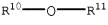
Reconsideration is requested of the rejection of claims 1-4, 6, 9, 10, and 15-25 under 35 U.S.C. §103(a) as being unpatentable over any one of the following combinations: Lambert (J. Applied Microbiol.) and Syverson (U.S. 5,612,045) in view of Pacini, et al. (U.S. 3,393,678) and Cunningham (U.S. 4,318,404) or unpatentable over Pacini, et al. (U.S. 3,393,678) in view of Cunningham (U.S. 4,318,404), Lambert (J. Applied Microbiol.)and Syverson (U.S. 5,612,045) or unpatentable over Cunningham (U.S. 4,318,404) in view of Lambert (J. Applied Microbiol.), Syverson (U.S. 5,612,045) and Pacini, et al. (U.S. 3,393,678).

Claim 1, as amended, is directed to an exoprotein inhibitor for inhibiting the production of exoproteins from Gram positive bacteria in and around a vagina. The exoprotein inhibitor comprises a non-absorbent substrate for insertion into the

vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. The non-absorbent substrate having deposited thereon an effective amount of a first active ingredient present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate, and an effective amount of a second active ingredient. The first active ingredient has the general formula:



wherein R^1 is $-OR^6OH$; R^6 is a divalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^2, R^3, and R^4 are independently selected from the group consisting of H, OH, COOH, and $-C(O)R^9$; R^9 is hydrogen or a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety. The second active ingredient has the general formula:



wherein R^{10} is a straight or branched alkyl or straight or branched alkenyl having from 8 to about 18 carbon atoms and R^{11} is selected from the group consisting of an alcohol, a polyalkoxylated sulfate salt and a polyalkoxylated sulfosuccinate salt. The first active ingredient and the second active ingredient are effective in inhibiting the production of exoprotein from Gram positive bacteria.

Lambert discloses a method of examining the effect of inoculum size on the degree of inhibition observed with respect

to inhibitor concentration. Specifically, the inoculum size dependencies of phenethyl alcohol, phenoxyethanol, p-chloro-mcresol,trichloro-phenol, thymol, and dodecyltrimethylammonium bromide against *S. aureus* were analyzed. For some inhibitors examined, such as dodecyltrimethylammonium bromide (C12QAC), it was found that at lower inoculum levels, there was a greater biocidal effect, whereas at higher inoculum levels, there was a greater degree of quenching of the biocide, causing the inhibitor to act more as a simple (sublethal) inhibitor. Lambert states that the method disclosed therein may be used to quantify the effect in the region between reversible and irreversible damage, or sublethal injury to cell death. Furthermore, Lambert states that the disclosed model suggests that on a molar basis, phenethyl alcohol is a better inhibitor than phenoxyethanol against *S. aureus*.

Significantly, however, as the Office recognizes on pages 2-3 of the instant final Office action, Lambert does not teach or suggest phenoxyethanol on a non-absorbent substrate and Lambert fails to teach the claimed non-absorbent tampon applicator. Further, Lambert does not teach or suggest a first active ingredient such as phenoxyethanol deposited on a non-absorbent substrate present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate. These are significant aspects of Applicants' amended claim 1.

Moreover, Applicants note that not all antibacterial compounds are appropriate for use in the vaginal area. For example, Applicants note that Lambert discloses that some antibacterial compounds exhibit biocidal effects against *S. aureus* which means that it could also kill the beneficial bacteria in the vaginal area. Conversely, Applicants' claimed

amounts of the effective ingredients are not harmful to the beneficial bacteria in the vaginal area. Thus, the mere disclosure that a compound has antibacterial properties against *S. aureus* is not, in and of itself, reason for one skilled in the art to use the compound in combination with a non-absorbent substrate for insertion into a vagina. What is important is that nowhere does Lambert discuss using its compounds in a vagina or the vaginal area. Accordingly, one skilled in the art would not be motivated to deploy the compounds disclosed in Lambert absent some suggestion that the antibacterial compounds would be present in an amount that would not be harmful to beneficial bacteria in the vaginal area.

Syverson is directed to **absorbent articles**, such as catamenial tampons, which include an effective amount of an ether compound to substantially inhibit the production of exotoxins by Gram positive bacteria. Specifically, the tampon contains an effective amount of the inhibiting ether compound to substantially inhibit the formation of TSST-1 when the tampon is exposed to *S. aureus* bacteria. The compositions can be prepared and applied in any suitable form, including aqueous solutions, lotions, balms, gels, salves, ointments, boluses, suppositories, and the like. The ether composition may additionally employ one or more pharmaceutically acceptable and compatible carrier materials useful for the desired application.

Significantly, however, as the Office recognizes on page 3 of the instant final Office action, while Syverson **only** teaches **absorbent tampons** and states that the tampon may or may not have an applicator, the instant claims require an applicator that is **non-absorbent**. The Office asserts that Syverson teaches including effective amounts of ether compounds and combinations

of other antimicrobial or antibacterial compounds (col. 5).[1] While Syverson teaches including effective amounts of ether compounds and combinations of other antimicrobial or antibacterial compounds, Syverson does not teach or suggest Applicants' first active ingredient deposited on a non-absorbent substrate present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate.

Recognizing the deficiencies of Lambert and Syverson, the Office cites Pacini, et al. and Cunningham references for combination with the Lambert and Syverson references in an attempt to arrive at each and every limitation of Applicants' claim 1.

Pacini, et al. disclose catamenial devices, such as tampons or vaginal inserts, and imparting upon them antibacterial qualities as well as physical lubricity that facilitates and lends comfort to their use. Specifically, Pacini, et al. disclose that polymetallic pectinates can be made into films or their dispersions may be sprayed on or applied to materials intended for vaginal tamponing. The coating is used to better facilitate the insertion into the vaginal vault. The advantages of the coating can include: (1) development of a gelatinous film that facilitates the introduction of the tampon or applicator; (2) liberation from the gel of galacturonic acid resulting from the destructive hydrolysis of the pectin; and, (3) liberation for diffusion over the mucosal surfaces of the vaginal vault of metal pectinates, which exert bactericidal and/or protozoicidal effectiveness.

[1] Office Action dated December 11, 2009, page 3.

Cunningham discloses an applicator for a tampon having a convolution so as to double the applicator upon itself to form parallel walls with the convolution there between. The applicator comprises a flexible sleeve about the tampon and overlaps a portion of the forward end of the tampon. Suitable materials for the sleeve include polyethylene or polypropylene. The sleeve may be coated with an appropriate lubricant.

In order for the Office to show a *prima facie* case of obviousness, M.P.E.P. §2142 requires a clear articulation of the reasons why the claimed invention would have been obvious. Specifically, the Supreme Court in KSR International Co. v. Teleflex Inc., 550 U.S. 398, 418, 82 USPQ2d 1385, 1396 (2007) noted that the burden lies initially with the Office to provide an explicit analysis supporting a rejection under 35 U.S.C. 103. "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." The Court in KSR International further identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966). Specifically, as previously required by the TSM (teaching, suggestion, motivation) approach to obviousness, one exemplary rationale indicated requires some teaching, suggestion, or motivation in the prior art reference that would have led one of ordinary skill to modify the prior art reference to arrive at the claimed invention. Specifically, to reject a claim based on this rationale, the Office must articulate the following: (1) a finding that there was some teaching, suggestion, or motivation, either in the reference itself or in

the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at each and every limitation of the claimed invention; (2) a finding that there was reasonable expectation of success; and (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. The Office has failed to meet its burden under number (1) above, as the cited references fail to show each and every limitation of Applicant's invention and there is no apparent reason for one skilled in the art to combine the reference teachings to arrive at each and every limitation. It simply would not have been obvious to one skilled in the art to arrive at Applicant's claimed combinations.

Specifically, nowhere in the cited references (or in the knowledge available to one skilled in the art) is there an apparent reason to combine the references to arrive at each and every limitation of Applicants' amended claim 1. As recognized by the Supreme Court in KSR International Co. v. Teleflex, Inc., while an obviousness determination is not a rigid formula, the TSM(teaching, suggestion, motivation) test captures a helpful insight: "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs [caution as to] a patent application that claims as innovation the combination of two known [elements] according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the [art] to combine the elements in the way the claimed new

invention does."[2]

Specifically, the combination of cited references fails to disclose or suggest an exoprotein inhibitor for inhibiting the production of exoproteins from Gram positive bacteria in and around the vagina comprising a non-absorbent substrate having deposited thereon an effective amount of the first active ingredient present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate, and an effective amount of the second active ingredient as required in Applicants' amended claim 1. In fact, none of the cited references disclose or suggest any amount of Applicants' first active ingredient, let alone disclose or suggest an amount of the first active ingredient present on a non-absorbent substrate.

At best, Syverson, et al. discloses that Applicants' second active ingredient can be present in an effective amount of 0.005 millimoles per gram of absorbent substrate.[3] This is not, however, a disclosure of Applicants' first active ingredient present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate. This is a significant aspect of Applicants' invention, as the amount of aromatic compound on the non-absorbent product significantly reduces the production of TSST-1 while remaining unharmful to beneficial bacteria in and around the vagina. As such, the combination of cited references fails to disclose or suggest each and every element of Applicants' amended claim 1, as is required for a *prima facie* case of obviousness.

[2] 2007 WL at 5.
[3] US 5612045, col 4, ln 43-45.

Moreover, nowhere in the cited references (or in the knowledge available to one skilled in the art) is there an apparent reason to combine the references to arrive at each and every limitation of Applicants' amended claim 1. Specifically, as noted above, none of the cited references disclose any amount of an aromatic compound as part of an exoprotein inhibitor, let alone from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate. As such, in order to arrive at the specific exoprotein inhibitor of Applicants' claim 1, one having ordinary skill in the art would have to randomly choose an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate of the first active ingredient to be present on the non-absorbent substrate. Without any disclosure of an amount of an aromatic compound or the significance thereof, it simply does not follow that it would be obvious to make such a modification/combination.

Applicants note that on page 8 of the current Final Office action, the Office asserts that Applicants are arguing against the references individually and that one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. Applicants note, however, that they have indeed argued against the combination of all four references cited against Applicants in the arguments made above. Applicants further note, however, that on page 2 of the current Final Office action, the Office has rejected the pending claims "over any one of the following combinations." Accordingly, as the Office has phrased the rejection in such a manner that could include "any combination"

of the cited references, Applicants' arguments below are made in reference to any possible combination of the cited references. That is, Applicants' arguments below are made to show that it would not be obvious for a person having ordinary skill in the art to make any of the possible combinations suggested by the Office on page 2 of the current Final Office action. As such, Applicants submit that, contrary to the Office's assertion, Applicants are not arguing against the references individually, but, rather, Applicants are arguing against the possibility of any combination of the cited references.

Specifically, there is no reason to combine Pacini, et al. with the other cited references. The Office suggests that since Pacini, et al. suggest that antimicrobial compounds may be employed in a tampon fabric itself or in the enclosure that holds the tampon that it would have been obvious to combine the teachings of Pacini, et al. with the phenoxyethanol of Lambert and the ether compounds as taught by Syverson in the tampon applicators of Cunningham because Lambert states that the compounds are effective in inhibiting *S. aureus* and Syverson suggests employing compounds for inhibiting toxic shock syndrome. Applicants respectfully disagree.

In particular, Applicants submit that there is no reason to combine Pacini, et al. with Lambert and Syverson because nowhere in Pacini, et al. is the inhibition of exoproteins ever discussed. That is, Pacini, et al. merely discloses that polymetallic pectinates or their dispersions can be placed onto a tampon as a coating to improve insertion. This is completely different, however, than depositing the first and second active ingredient of Applicants' claim 1 (or the phenoxyethanol of Lambert and the ethers of Syverson) onto a non-absorbent substrate in order to inhibit the production of exoproteins from

Gram positive bacteria, as is required by Applicants' claim 1. In particular, why would one having ordinary skill in the art, when looking to improve insertability with a coating of polymetallic pectinates, as disclosed by Pacini, et al., look to Lambert and Syverson, which disclose completely separate and distinct compounds that inhibit the production of exoproteins from Gram positive bacteria. Particularly, why would one having ordinary skill in the art make such a combination when nowhere in Pacini, et al. are the first active ingredients of Applicants' claimed invention (such as the phenoxyethanol of Lambert) or the second active ingredients of Applicants' claimed invention (such as the ethers of Syverson) taught or suggested? One simply would not, and could not, make such a combination.

Additionally, in the Response to Arguments section of the current Final Office action, on pages 8-9, the Office asserts that even though Pacini, et al. does not require inhibiting exoproteins; that applying a known technique to a known device to yield predictable results would be predictable to one having ordinary skill in the art. Applicants disagree with this assessment, as since nowhere in Pacini, et al. are exoproteins from Gram positive bacteria ever mentioned, or the importance of their inhibition thereof, it simply cannot be stated that one having ordinary skill in the art would find the combination of Pacini, et al. with that of Syverson, Lambert and Cunningham to yield predictable results. It simply cannot be stated that it would be obvious to make such a combination. This is particularly true in the instant case, where Syverson already discloses active ingredients that can be deposited on an absorbent tampon to inhibit exoprotein production from Gram positive bacteria. The Office has simply not proffered any evidence why it would be obvious to combine the cited references

other than the conclusory statement that such results would be "predictable."

Further, there is no reason to combine Pacini, et al., Lambert and Syverson with Cunningham in order to arrive at the exoprotein inhibitor of Applicants' claim 1. Initially, Applicants note that nowhere does Cunningham ever mention depositing any antimicrobial/antibacterial substance on its non-absorbent applicator, or the importance thereof. Why, then, would one having ordinary skill in the art look to combine Cunningham with the cited references to arrive at the exoprotein inhibitor comprising the non-absorbent substrate of Applicants' claim 1? There is simply no reason to modify the cited references to include the non-absorbent applicator of Cunningham.

Specifically, in order to arrive at the exoprotein inhibitor of Applicants' claim 1, one having ordinary skill in the art would first have to modify Pacini, et al. to include a composition that inhibits exoproteins, when nowhere does Pacini, et al. discuss exoprotein inhibitors at all, let alone exoprotein inhibitors for inhibiting the production of Gram positive bacteria. Then, one would have to select the phenoxyethanol of Lambert and the ethers of Syverson despite the fact that Lambert teaches phenoxyethanol as only one of several compounds that can inhibit *S. aureus*, and further, teaches phenethyl alcohol as a better inhibitor than phenoxyethanol. Further, Lambert does not disclose or suggest combining phenoxyethanol as a first active ingredient with any other active ingredient much less combining phenoxyethanol present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate with a second active ingredient such as the ether

compounds of Syverson. As aforementioned, Syverson also does not suggest, teach or disclose a first active ingredient present in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate to be combined with its ether compounds.

Further, one having ordinary skill in the art would then have to combine the cited references with the non-absorbent applicator of Cunningham, when none of the cited references, including Cunningham, disclose or suggest depositing antimicrobial/antibacterial compounds onto a **non-absorbent** tampon applicator.

Finally, one would have to then have to randomly select an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate of Applicants' first active ingredient to be placed on a non-absorbent substrate, when nowhere does the combination of references ever disclose or suggest **any** amounts. As noted above, one would have to make all of these modifications/combinations without using Applicants' disclosure as a blueprint. Applicants respectfully submit that it cannot be stated that it would be obvious to do so.

For the reasons set forth above, it is not foreseeable or predictable that one skilled in the art would simply modify/combine the phenoxyethanol of Lambert, in an amount of from about 0.5 micromoles per gram of non-absorbent substrate to about 100 micromoles per gram of non-absorbent substrate, with an effective amount of a second active ingredient, such as the ethers of Syverson, onto a non-absorbent substrate, such as the tampon or applicator of Pacini or the non-absorbent applicator of Cunningham, to arrive at the specific exoprotein inhibitor of Applicants' amended claim 1.

As none of the cited references teach or suggest each and every limitation as set forth in amended claim 1, amended claim 1 is patentable over the combination of Lambert, Syverson, Pacini, and Cunningham.

Claims 2-4, 6, 9, 10 and 15-25 depend from amended claim 1 and are thus patentable over the cited references for the same reasons set forth above for amended claim 1, as well as for the additional limitations they require.

Conclusion

In view of the above, Applicants respectfully request favorable reconsideration and allowance of all pending claims. The Commissioner is hereby authorized to charge any fee deficiency in connection with this Amendment C and Response After RCE to Deposit Account Number 01-2384.

Respectfully Submitted,

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